

WHAT IS CLAIMED IS:

1. A process of treating oral leukoplakia lesions of humans in need of such treatment, the process comprising the step of applying topically to the leukoplakia lesion an effective amount of a clear aqueous formulation comprising:

water;

a water miscible pharmaceutically acceptable polyol;

a pharmaceutically acceptable unsaturated fatty acid ester;

a pharmaceutically acceptable surfactant, and

$\beta$ -carotene, said  $\beta$ -carotene being in a micellized form within said formulation.

2. A process in accordance with Claim 1 wherein the formulation additionally comprises a pharmaceutically acceptable anti-oxidant.

3. A process in accordance with Claim 2 wherein the pharmaceutically acceptable anti-oxidant is d-alpha-tocopherol or a pharmaceutically acceptable derivative of d-alpha tocopherol having vitamin E activity.

4. A process in accordance with Claim 1 wherein the formulation additionally comprises a compound having vitamin A activity.

5. A process in accordance with Claim 1 wherein the surfactant is polyethoxylated castor oil.

1           6. A process in accordance with Claim 1 wherein the polyol is  
2 glycerol.

3           7. A process in accordance with Claim 1 wherein the unsaturated fatty  
4 acid ester is ethyl linoleate.

5           8. A process in accordance with Claim 1 wherein the formulation is a  
6 gel.

7           9. A process in accordance with Claim 8 comprising the steps of  
8 applying the gel to the leukoplakia lesion at least twice a day.

9           10. A process in accordance with Claim 1 wherein the formulation  
10 comprises:

11           10 to 50 % by weight water;

12           5 to 40 % by weight of the water miscible pharmaceutically acceptable  
13 polyol;

14           1 to 20 % by weight of the pharmaceutically acceptable unsaturated  
15 fatty acid ester;

16           10 to 60 % by weight of the pharmaceutically acceptable surfactant,  
17 and

18           0.03 to 9.0 % by weight of  $\beta$ -carotene.

19           11. A process in accordance with Claim 10 wherein the water miscible  
20 pharmaceutically acceptable polyol is glycerol;

1 the pharmaceutically acceptable unsaturated fatty acid ester is ethyl  
2 linoleate, and

3 the pharmaceutically acceptable surfactant is polyethoxylated castor oil.

4 12. A process in accordance with Claim 1 wherein the formulation  
5 comprises:

6 20 to 40 % by weight water;

7 10 to 30 % by weight of the water miscible pharmaceutically  
8 acceptable polyol;

9 1 to 15 % by weight of the pharmaceutically acceptable unsaturated  
10 fatty acid ester;

11 20 to 40 % by weight of the pharmaceutically acceptable surfactant,  
12 and

13 0.3 to 3.0 % by weight of  $\beta$ -carotene.

14 13. A process in accordance with Claim 12 wherein the water miscible  
15 pharmaceutically acceptable polyol is glycerol;

16 the pharmaceutically acceptable unsaturated fatty acid ester is ethyl  
17 linoleate, and

18 the pharmaceutically acceptable surfactant is polyethoxylated castor oil.

19 14. A process in accordance with Claim 13 wherein the formulation  
20 additionally comprises d-alpha-tocopherol and a compound having vitamin A

activity.

15. A process in accordance with Claim 14 wherein the formulation is a gel.

16. A process in accordance with Claim 15 comprising the steps of applying the gel to the leukoplakia lesion at least twice a day.

17. A process in accordance with Claim 1 wherein the formulation comprises:

50 to 95 % by weight water;

1 to 10 % by weight of the water miscible pharmaceutically acceptable polyol;

0.01 to 2 % by weight of the pharmaceutically acceptable unsaturated fatty acid ester;

0.01 to 5 % by weight of the pharmaceutically acceptable surfactant, and

0.003 to 1.2 % by weight of  $\beta$ -carotene,

1 to 10 % by weight of a pharmaceutically acceptable sweetener;

0.01 to 2% of a pharmaceutically acceptable antibacterial agent;

d -alpha tocopherol or a pharmaceutically acceptable derivative of d-alpha tocopherol having vitamin E activity;

1 vitamin A palmitate or a pharmaceutically acceptable derivative of  
2 vitamin A palmitate having vitamin A activity;  
3 a pharmaceutically acceptable chelating agent;  
4 a pharmaceutically acceptable antifoaming agent;  
5 a flavoring agent, and  
6 a preservative.

7 18. A process in accordance with Claim 17 wherein the water miscible  
8 pharmaceutically acceptable polyol is glycerol;

9 the pharmaceutically acceptable unsaturated fatty acid ester is ethyl  
10 linoleate;

11 the pharmaceutically acceptable surfactant is polyethoxylated castor  
12 oil;

13 the pharmaceutically acceptable sweetener is xylitol;

14 the pharmaceutically acceptable antibacterial agent is cetyl pyridinium  
15 chloride;

16 the pharmaceutically acceptable chelating agent is disodium EDTA,  
17 and

18 the preservative is sodium benzoate.

19 19. A process in accordance with Claim 18 wherein the formulation is  
20 an oral rinse.

1                   20. A process in accordance with Claim 19 wherein the formulation  
2 comprises:

3                   75 to 95 % by weight water;  
4                   2 to 7 % by weight of glycerol;  
5                   0.01 to 0.5 % by weight ethyl linoleate;  
6                   0.01 to 1 % by weight polyethoxylated castor oil;  
7                   0.003 to 10.6 % by weight of  $\beta$ -carotene,  
8                   2 to 7 % by weight of xylitol;  
9                   0.01 to 1 % of cetyl pyridinium chloride;  
10                  0.005 to 0.05 % by weight of disodium EDTA;  
11                  0.2 to 1.5 % by weight of flavoring agent, and  
12                  0.01 to 0.5 % by weight of sodium benzoate.

13                  21. A clear aqueous composition for topical application in the oral  
14 cavity of humans, the composition comprising:  
15 water;  
16 a water miscible pharmaceutically acceptable polyol;  
17 a pharmaceutically acceptable unsaturated fatty acid ester;  
18 a pharmaceutically acceptable surfactant, and  
19  $\beta$ -carotene, said  $\beta$ -carotene being in a micellized form within said  
20 composition.

22. A composition in accordance with Claim 21 wherein the composition additionally comprises a pharmaceutically acceptable anti-oxidant.

23. A composition in accordance with Claim 22 wherein the pharmaceutically acceptable anti-oxidant is d-alpha-tocopherol or a pharmaceutically acceptable derivative of d-alpha tocopherol having vitamin E activity.

24. A composition in accordance with Claim 21 wherein the composition additionally comprises a compound having vitamin A activity.

25. A composition in accordance with Claim 21 wherein the surfactant is polyethoxylated castor oil.

26. A composition in accordance with Claim 21 wherein the polyol is glycerol.

27. A composition in accordance with Claim 21 wherein the unsaturated fatty acid ester is ethyl linoleate.

28. A composition in accordance with Claim 21 wherein the composition is a gel.

29. A composition in accordance with Claim 21 wherein the composition comprises:

10 to 50 % by weight water;



5 to 40 % by weight of the water miscible pharmaceutically acceptable polyol;

1 to 20 % by weight of the pharmaceutically acceptable unsaturated fatty acid ester;

10 to 60 % by weight of the pharmaceutically acceptable surfactant, and

0.03 to 9.0 % by weight of  $\beta$ -carotene.

30. A composition in accordance with Claim 29 wherein the water miscible pharmaceutically acceptable polyol is glycerol;

the pharmaceutically acceptable unsaturated fatty acid ester is ethyl linoleate, and

the pharmaceutically acceptable surfactant is polyethoxylated castor oil.

31. A composition in accordance with Claim 21 wherein the composition comprises:

20 to 40 % by weight water;

10 to 30 % by weight of the water miscible pharmaceutically acceptable polyol;

1 to 15 % by weight of the pharmaceutically acceptable unsaturated fatty acid ester;

20 to 40 % by weight of the pharmaceutically acceptable surfactant, and



0.3 to 3.0 % by weight of  $\beta$ -carotene.

**32.** A composition in accordance with Claim 31 wherein the water miscible pharmaceutically acceptable polyol is glycerol;

the pharmaceutically acceptable unsaturated fatty acid ester is ethyl linoleate, and

the pharmaceutically acceptable surfactant is polyethoxylated castor oil.

**33.** A composition in accordance with Claim 32 wherein the composition additionally comprises d-alpha-tocopherol and a compound having vitamin A activity.

**34.** A composition in accordance with Claim 33 wherein the composition is a gel.

**35.** A composition in accordance with Claim 21 wherein the composition comprises:

50 to 95 % by weight water;

1 to 10 % by weight of the water miscible pharmaceutically acceptable polyol;

0.01 to 2 % by weight of the pharmaceutically acceptable unsaturated fatty acid ester;

0.01 to 5 % by weight of the pharmaceutically acceptable surfactant, and

0.003 to 1.2 % by weight of  $\beta$ -carotene,  
1 to 10 % by weight of a pharmaceutically acceptable sweetener;  
0.01 to 2% of a pharmaceutically acceptable antibacterial agent;  
d -alpha tocopherol or a pharmaceutically acceptable derivative of d-  
alpha tocopherol having vitamin E activity;  
vitamin A palmitate or a pharmaceutically acceptable derivative of  
vitamin A palmitate having vitamin A activity;  
a pharmaceutically acceptable chelating agent;  
a pharmaceutically acceptable antifoaming agent;  
a flavoring agent, and  
a preservative.

36. A composition in accordance with Claim 35 wherein the water  
miscible pharmaceutically acceptable polyol is glycerol;  
the pharmaceutically acceptable unsaturated fatty acid ester is ethyl  
linoleate;  
the pharmaceutically acceptable surfactant is polyethoxylated castor  
oil;  
the pharmaceutically acceptable sweetener is xylitol;  
the pharmaceutically acceptable antibacterial agent is cetyl pyridinium  
chloride;  
the pharmaceutically acceptable chelating agent is disodium EDTA,

and

the preservative is sodium benzoate.

37. A composition in accordance with Claim 36 wherein the composition is an oral rinse.

38. A composition in accordance with Claim 37 wherein the composition comprises:

75 to 95 % by weight water;

2 to 7 % by weight of glycerol;

0.01 to 0.5 % by weight ethyl linoleate;

0.01 to 1 % by weight polyethoxylated castor oil;

0.003 to 10.6 % by weight of  $\beta$ -carotene,

2 to 7 % by weight of xylitol;

0.01 to 1 % of cetyl pyridinium chloride;

0.005 to 0.05 % by weight of disodium EDTA;

0.2 to 1.5 % by weight of flavoring agent, and

0.01 to 0.5 % by weight of sodium benzoate.

39. A clear aqueous gel composition for topical application in the oral cavity of humans, the composition having been prepared by a process comprising the steps of:

admixing a suspension of  $\beta$ -carotene in edible oil with polyethoxylated

1 castor oil and heating said admixture to approximately 160 to 180 °C and  
2 agitating said admixture in said temperature range of 160 to 180 °C until a  
3 clear homogeneous solution is obtained;

4 thereafter cooling said admixture to approximately 130 to 135 °C and  
5 adding d-alpha-tocopherol, glycerol and ethyl linoleate to said admixture, the  
6 d-alpha-tocopherol, glycerol and ethyl linoleate being added to the admixture  
7 at such a rate of addition that the temperature of the resulting mixture is  
8 cooled to approximately 85 to 95 ° C;

9 maintaining the resulting mixture under agitation at 85 to 95° C until a  
10 clear homogeneous mixture is obtained;

11 thereafter adding under agitation water of approximately 55 to 60°C  
12 temperature and cooling the mixture under agitation until a clear homogenous  
13 product is obtained.

14 40. A clear aqueous gel composition in accordance with Claim 39  
15 comprising:

16 20 to 40 % by weight water;

17 10 to 30 % by weight of glycerol;

18 1 to 15 % by weight of ethyl linoleate;

19 20 to 40 % by weight of polyethoxylated castor oil;

20 0.3 to 3.0 % by weight of  $\beta$ -carotene.  
21